

Diabetic Retinopathy

John H. Drouilhet MD

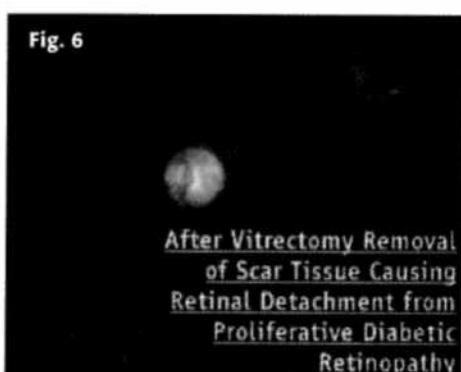
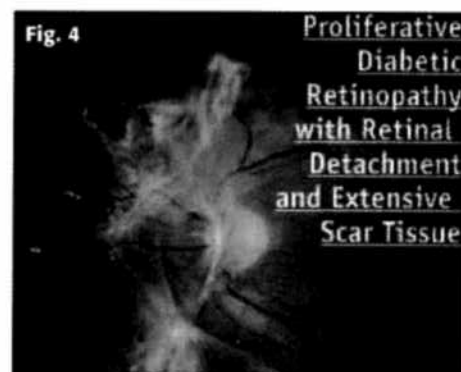
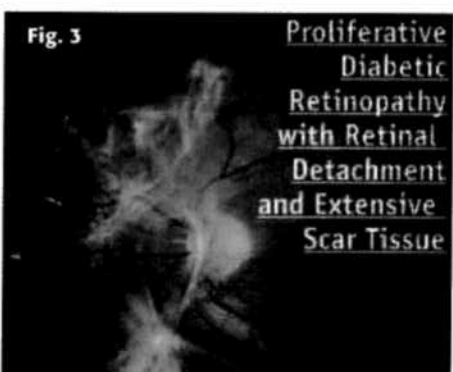
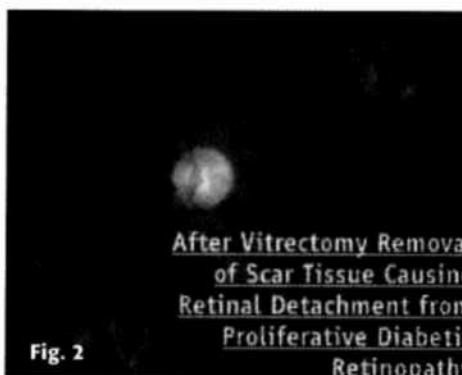
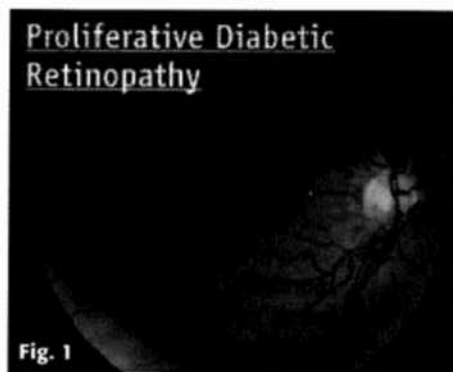
Diabetic Retinopathy is the leading cause of new blindness in the 25 to 74 year age group in the United States. The diabetic patient has a twenty-five times greater risk of developing blindness than the non-diabetic patient. Only 50 % of all patients with diabetes mellitus have actually been diagnosed.¹ The Community Epidemiologic Work Group for Diabetes Mellitus in Hawaii showed a prevalence of 25.2 per 1000 to 63 per 1000 persons based on self-reported data. The State Blind Registry for 1992-1993 showed diabetic retinopathy as the second leading cause of all new blind cases (20.9%).² Diabetic retinopathy is a significant cause for concern in Hawaii in regard to patient quality of life and socioeconomic concerns.

Various factors have been studied in the pathophysiology of Diabetic Retinopathy to include aldose reductase, growth hormone, blood rheology abnormalities, blood viscosity,¹ vascular endothelial growth factor,³ etc. It is as yet not fully understood how much each of these (or other unknown factors) contributes to the retinal vascular disease process.

Duration of diabetes mellitus is critical relative to the onset of retinopathy. Type I diabetics usually have no retinopathy until five years after diagnosis. By 15 years into the disease 90% will have retinopathy. Type II diabetics can present with retinopathy on initial diagnosis. The recommendation for dilated eye examination in the Type I diabetic is yearly once the patient has had diabetes for five years. Type II diabetics should be examined yearly from time of diagnosis.¹

Definite risk factors for diabetic retinopathy include duration of disease, poor glucose control, hypertension, and renal disease.⁴ As 87% of patients with advanced retinopathy have nephropathy and/or neuropathy, patients with nephropathy and/or neuropathy definitely need an ophthalmologic exam.⁵

Diabetic Retinopathy has two major classifications—Non-Proliferative Diabetic Retinopathy (NPDR) and Proliferative Diabetic Retinopathy (PDR).¹ In NPDR one sees retinal microaneurysms, dot hemorrhages, cotton wool spots, intraretinal microvascular abnormalities, and retinal edema (Fig 1). Edema affecting the



macula causes loss of central (reading) vision. PDR is the more advanced stage occurring when the retina starts to lose its blood supply. The eye responds by growing new blood vessels on the optic nerve or retina (Fig 2). These fragile new vessels bleed, filling the vitreous cavity. Scar tissue accompanies the neovascularization and can cause retinal detachment (Fig 3).

To combat Diabetic Retinopathy, surgical strategies were developed in which Laser surgery treats macular edema and causes atrophy of the neovascularization. Vitrectomy surgery removes

Benzamycin®
(erythromycin-benzoyl peroxide topical gel)
Topical gel: erythromycin (3%), benzoyl peroxide (5%)
For Dermatological Use Only – Not for Ophthalmic Use
Reconstitute Before Dispensing

Brief Summary—Consult package insert for full prescribing information.

INDICATIONS AND USAGE

BENZAMYCIN® Topical Gel is indicated for the topical treatment of acne vulgaris.

CONTRAINDICATIONS

BENZAMYCIN® Topical Gel is contraindicated in those individuals who have shown hypersensitivity to any of its components.

WARNINGS

Pseudomembranous colitis has been reported with nearly all antibacterial agents, including erythromycin, and may range in severity from mild to life-threatening. Therefore, it is important to consider this diagnosis in patients who present with diarrhea subsequent to the administration of antibacterial agents.

Treatment with antibacterial agents alters the normal flora of the colon and may permit overgrowth of clostridia. Studies indicate that a toxin produced by *Clostridium difficile* is one primary cause of "antibiotic-associated colitis."

After the diagnosis of pseudomembranous colitis has been established, therapeutic measures should be initiated. Mild cases of pseudomembranous colitis usually respond to drug discontinuation alone. In moderate to severe cases, consideration should be given to management with fluids and electrolytes, protein supplementation and treatment with an antibacterial drug clinically effective against *C. difficile* colitis.

PRECAUTIONS

General: For topical use only; not for ophthalmic use. Concomitant topical acne therapy should be used with caution because a possible cumulative irritancy effect may occur, especially with the use of peeling, desquamating or abrasive agents. If severe irritation develops, discontinue use and institute appropriate therapy.

The use of antibiotic agents may be associated with the overgrowth of nonsusceptible organisms including fungi. If this occurs, discontinue use and take appropriate measures.

Avoid contact with eyes and all mucous membranes.

Information for Patients: Patients using BENZAMYCIN® Topical Gel should receive the following information and instructions: 1. This medication is to be used as directed by the physician. It is for external use only. Avoid contact with the eyes, nose, mouth, and all mucous membranes.

2. This medication should not be used for any disorder other than that for which it was prescribed.

3. Patients should not use any other topical acne preparation unless otherwise directed by physician.

4. Patients should report to their physician any signs of local adverse reactions.

5. BENZAMYCIN® Topical Gel may bleach hair or colored fabric.

6. Keep product refrigerated and discard after 3 months.

CARCINOGENESIS, MUTAGENESIS AND IMPAIRMENT OF FERTILITY

Data from a study using mice known to be highly susceptible to cancer suggests that benzoyl peroxide acts as a tumor promoter. The clinical significance of this is unknown.

No animal studies have been performed to evaluate the carcinogenic and mutagenic potential or effects on fertility of topical erythromycin. However, long-term (2-year) oral studies in rats with erythromycin ethylsuccinate and erythromycin base did not provide evidence of tumorigenicity. There was no apparent effect on male or female fertility in rats fed erythromycin (base) at levels up to 0.25% of diet.

Pregnancy: Teratogenic Effects: Pregnancy CATEGORY C: Animal reproduction studies have not been conducted with BENZAMYCIN® Topical Gel or benzoyl peroxide.

There was no evidence of teratogenicity or any other adverse effect on reproduction in female rats fed erythromycin base (up to 0.25% diet) prior to and during mating, during gestation and through weaning of two successive litters.

There are no well-controlled trials in pregnant women with BENZAMYCIN® Topical Gel. It also is not known whether BENZAMYCIN® Topical Gel can cause fetal harm when administered to a pregnant woman or can affect reproductive capacity. BENZAMYCIN® Topical Gel should be given to a pregnant woman only if clearly needed.

Nursing Women: It is not known whether BENZAMYCIN® Topical Gel is excreted in human milk after topical application. However, erythromycin is excreted in human milk following oral and parenteral erythromycin administration. Therefore, caution should be exercised when erythromycin is administered to a nursing woman.

Pediatric Use: Safety and effectiveness of this product in pediatric patients below the age of 12 have not been established.

ADVERSE REACTIONS

In controlled clinical trials, the total incidence of adverse reactions associated with the use of BENZAMYCIN® Topical Gel was approximately 3%. These were dryness and urticarial reaction.

The following additional local adverse reactions have been reported occasionally: irritation of the skin including peeling, itching, burning sensation, erythema, inflammation of the face, eyes and nose, and irritation of the eyes. Skin discoloration, oiliness and tenderness of the skin have also been reported.

DOSAGE AND ADMINISTRATION

BENZAMYCIN® Topical Gel should be applied twice daily, morning and evening, or as directed by a physician, to affected areas after the skin is thoroughly washed, rinsed with warm water and gently patted dry.

Important to the Pharmacist

Prior to dispensing, tap vial until powder flows freely. Add indicated amount of ethyl alcohol (70%) to vial (to the mark) and immediately shake to completely dissolve erythromycin. Add this solution to gel and stir until homogeneous in appearance (1 to 1½ minutes). BENZAMYCIN® Topical Gel should then be stored under refrigeration. Do not freeze. Place a 3-month expiration date on the label.

NOTE: Prior to reconstitution, store at room temperature between 15° and 30°C (59° – 86°F).

After reconstitution, store under refrigeration between 2° and 8°C (36° – 46°F).

Do not freeze. Keep tightly closed. Keep out of the reach of children.


Caution: Federal (U.S.A.) law prohibits dispensing without prescription.

U.S. Patent Nos. 4,387,107 and 4,497,794.

Manufactured by Rhône-Poulenc Rorer Puerto Rico Inc.

Manati, Puerto Rico

For **DERMIK LABORATORIES, INC.**
A Rhône-Poulenc Rorer Company
Collegeville, PA 19426

 **DERMIK LABORATORIES, INC.**
Dedicated to Dermatology®
A RHÔNE-POULENC RORER COMPANY

Rev. 12/95

IN-7121N

Volunteers Needed

• Volunteers with medical knowledge needed to staff and man the library and a call-in telephone information line. These people would be trained by the American Cancer Society, and would be responsible for giving out cancer information to walk-ins and callers. For further info, call Susan Jacobs at the American Cancer Society, 595-7500 ext. 202



dense vitreous hemorrhage and relieves traction retinal detachment from scarring.

The Early Treatment Diabetic Retinopathy Study (ETDRS)⁶ demonstrated a 50% reduction in loss of vision with appropriate laser surgery for clinically significant macular edema (Fig 4). This study also showed that aspirin did not reduce progression of diabetic retinopathy nor increase the risk of vision loss from vitreous hemorrhage.⁷ The Diabetic Retinopathy Study showed a 50-60% reduction in vision loss for timely laser surgery in patients with Proliferative Diabetic Retinopathy (Fig 5).⁸ The Diabetic Retinopathy Vitrectomy Study showed better visual result with early vitrectomy surgery in Type I Diabetics with nonclearing vitreous hemorrhage (Fig 6).⁹

The Diabetes Control and Complications Trial (DCCT) showed delay in onset and slower progression of Diabetic Retinopathy, nephropathy, and neuropathy. There was a 50% reduction in amount of laser surgery for Diabetic Retinopathy in tightly controlled diabetics.¹⁰

Diabetic Retinopathy is the major cause of new blindness in working Americans. The longer the duration of diabetes, the greater the risk of retinopathy. Excellent serum glucose, blood pressure, and cholesterol control delay and decrease the severity of retinopathy. Timely laser surgery reduces vision loss by 50%. It is the responsibility of all physicians in partnership to diagnose and properly manage the diabetic patient.

References

1. Benson WE, Tasman W, Duane TD. Diabetes Mellitus and the Eye in Duane's Ophthalmology. Ed. Tasman W, Jaeger EA. Duane's Ophthalmology CD-ROM Edition, 1996.
2. Wood DW., Uyeda C, Yerkes J. Community Epidemiology Work Group for Diabetes Mellitus 1993 Monograph, 1994.
3. Pe'er J, Folberg R, Ilit A, et al. Upregulated expression of vascular endothelial growth factor in proliferative diabetic retinopathy. *Br J Ophthalmol* 1996; 80(3): 241-245.
4. Okada S, Ichiki K, Tanokuchi S, et al. Factors related to the development and progression of diabetic retinopathy in patients with type II diabetes. *J Int Med Res* 1996;24(2): 214-220.
5. Delcourt C, Villaatte-Cathelineau B, Vauzelle-Kervroedan F, et al. Clinical correlates of advanced retinopathy in type II diabetic patients: implications for screening. The DODIAB-INSEEM-Zeneca Pharma Study Group. *J Clin Epidemiol* 1996;49(6): 679-685.
6. Early Treatment of Diabetic Retinopathy Study Research Group: Photocoagulation for diabetic macular edema. *Arch Ophthalmol* 1985; 103: 1796-1806.
7. Early Treatment of Diabetic Retinopathy Study Research Group: Effects of aspirin treatment on diabetic retinopathy. ETDRS report #8. *Ophthalmology* 1991; 98(suppl):757-765.
8. Diabetic Retinopathy Study Research Group: Four risk factors for severe visual loss in diabetic retinopathy: the third report from the Diabetic Retinopathy Study. *Arch Ophthalmol* 1979; 97: 654-666.
9. Diabetic Retinopathy Study Research Group: Early vitrectomy for severe proliferative diabetic retinopathy in eyes with useful vision: Clinical applications of results of a randomized trial. DRVS report #4. *Ophthalmology* 1988; 95: 1321-1334.
10. Diabetes Control and Complications Trial Research Group: The effects of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. *N Engl J Med* 1993; 329: 977-986.
11. Chew EY, Klieg ML, Ferris FL, et al. Diabetic Retinopathy Study Research Group Association of elevated serum lipids with retinal hard exudate in diabetic retinopathy. *Arch Ophthalmol* 1996; 114: 1079-1084.